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No. 7.—Recent Advances in Therapeutic Agents for Veterinary Use*

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INTRODUCTION.

At no time can the responsibility of preparing a paper, for presentation to the Annual Congress of the National Veterinary Medical Association, be lightly undertaken, but it seems that special responsibilities are attached to the preparation of a paper dealing with Therapeutic Agents, since any claims made for such agents, without due substantiation, might lead to their indiscriminate employment, with disastrous results, unless these claims were adequately confounded during the discussion that took place on the paper.

In preparing such a paper, there is a choice of courses open to the author. *Either* he may choose to describe agents that have already been extensively tried in veterinary practice and by provoking a discussion on them, may elicit a concensus of opinion on their true value. *Or* the author may discuss new discoveries in the realm of general therapeutics, some of which may have been employed on an experimental basis in veterinary practice, with the object of placing these discoveries before the Congress so that discussion may show the lines along which these discoveries might be applied in the field. It is the latter course that I have decided to adopt in preparing this paper.

One of the great difficulties that attends the introduction of new drugs is that of assessing their value in the field. Large scale field experiments are of necessity very costly, and are seldom possible in naturally occurring disease.

A remedy may be tried out in an outbreak of a particular disease, but under ordinary conditions of practice it is unlikely that adequate controls can be obtained for the accurate evaluation of apparent results. This difficulty of reliable assessment of the value of new discoveries leads to what might be described as "fashions in drugs." So we see a remedy, newly introduced, being extensively used and then, after a brief period, it largely falls into disuse. A few remedies prove of some real value, and after a time find their proper place in the pharmacopoeia. It is particularly in respect of diseases for which there is no specific remedy that this train of events is apt to occur.

To a large extent, the only trial available for new discoveries is by means of small laboratory animals. Some of these may be susceptible to certain diseases of farm animals, and may afford a possible index of the likelihood of a particular substance proving of value in a specific condition. Unfortunately, results obtained in small laboratory animals may not be repeated when the drug is utilised on the normal victim of the disease. In addition, the toxicity of the agent may be entirely different in the two species of animals employed. When the disease concerned cannot be produced in laboratory animals, and the drug has to be employed merely because of pharmacological results obtained in comparable diseases in small experimental animals, the possibility of error and ultimate disappointment is greatly increased.

At the same time, it is necessary to emphasise that new remedies are not infrequently unjustly condemned and discarded because they have not been properly applied in the conditions for which they have been recommended.

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Bevan emphasises this point very adequately in a reference to the use of trypan blue.[1]

In deciding which substances to discuss in this paper, it has been thought preferable to discuss reasonably thoroughly relatively few drugs, rather than to skim briefly over a much greater number. But it will be realised that the limits of such a paper as this preclude a complete discussion of any individual substance.

The Sulphanilamide Group

General Pharmacology.

At the present moment no paper on recent advances in therapeutic agents would fulfil its purpose if it did not deal at least adequately with the drugs that constitute the sulphanilamide group.

The discovery of this group of drugs represented the successful culmination of a long search for remedies that would have comparable effects on streptococci to those obtained with the parasite of malaria by the use of quinine and the causal agent of syphilis with salvarsan.

At the present moment the sulphanilamide group attract more attention than any other group of drugs, and it is easy to be dazzled by the brilliance of the success that they have achieved in the treatment of certain diseases, and this makes it all the more important that care should be exercised that they are properly employed.

The first substance of this group that attracted general attention was prontosil. In laboratory animals it was found to be relatively non-toxic and pharmacologically inert in regard to blood pressure and blood vessels, but mice inoculated intraperitoneally with 10 M.L.D. of *Streptococcus pyogenes* survived if from 1/10 to 1/50 of the maximum tolerated dose was administered either orally or by injection. Prontosil is entirely without action on bacteria *in vitro* and its mode of action was for a time a mystery. The exact mechanism by which the sulphanilamides act is not yet clearly explained.

It appears to have been established that the action of prontosil is dependent on that portion of the compound which may be liberated in the body, namely p-amino-benzene-sulphonamide, now known as sulphanilamide. Pharmacological studies have been concentrated on sulphanilamide itself, and many compounds associated with it. Sulphanilamide is rapidly absorbed from the alimentary canal, absorption being complete in four hours. It is now known that sulphanilamide is not absorbed any more rapidly if given subcutaneously. Studies of absorption curves show that a maximum concentration in the blood is reached in about three hours, and if one dose only is given, the concentration curve falls in a straight line to almost nothing in the course of 24 hours.

The significance of these points does not appear to have been realised by many who have been using sulphanilamide drugs in veterinary practice. The therapeutic action of any single dose, provided that dose was sufficient to obtain the desired concentration in the blood, could only persist for about six hours. It is therefore necessary, if the action of the drug is to be maintained, that administration must be repeated in from four to six hours. It is most unlikely that one single dose will cure any serious infection. Sulphanilamide is excreted by the urine, and it is believed that 70 to 80 per cent. of the drug in the glomerular filtrate is reabsorbed; therefore the administration of large quantities of fluid will have the effect of washing the drug out of the body. Impairment of renal function may lead to its retention in the body.

Sulphanilamide is uniformly distributed throughout most tissues in the body, the concentration in the cerebrospinal fluid, however, is only about three-quarters of that in the blood.

It appears that before the desired results can be obtained in the treatment of disease, a concentration in the blood of 1 in 10,000, *i.e.* 10 mgs. per 100 c.c. of blood, is necessary.

In certain reports of the use of the drug in veterinary practice, the dose employed would be far too small to produce anything approaching this concentration. In suitable cases with this concentration some response may be expected in from two to three days. There is evidence that a course of more than ten days should never be given without a rest period. The method of giving single doses at intervals of several days has no pharmacological basis.

It cannot be too strongly emphasised that the sulphanilamide drugs are not "cure-alls." They are known to have actions against certain organisms. If these organisms are known to be constantly associated with a specific disease, then their use in the treatment of that disease is justified. But in non-specific disease with a varying bacterial picture, it is much more difficult to assess their real value, and in many instances it is very doubtful if they can be of any value.

Very extensive investigations have been conducted with a view to determining the mode of action of the sulphanilamide drugs in bacterial infections. The present state of knowledge regarding the actions was discussed fully by McIntosh and Whitby[2]. The summary of their publication puts the position very clearly:—

"Sulphanilamide drugs do not stimulate leucocytic or phagocytic activity.

"Sulphanilamide drugs do not affect the speed of production or the quantity and quality of specific immune bodies.

"Sulphanilamide drugs, both *in vivo* and *in vitro*, are not instantly active, and there is a quantity relationship between the effective dose of the drug and the number of bacteria affected.

"Sulphanilamide drugs are not simple germicides.

"Sulphanilamide drugs probably act by neutralisation of some metabolic function or enzymatic activity."

An interesting observation quoted by Garrod[3] was to the effect that the blood of patients receiving sulphanilamide is actually bactericidal, the active agent being in the serum.

Following the introduction of prontosil (sulphamo-chrysoidin) there were produced in this country compounds such as proseptasine (p. benzylaminobenzene sulphonamide) and soluseptasine (a soluble sodium compound with similar actions to proseptasine). These were found to be more generally useful than prontosil, possessing the desired therapeutic effects, but both having much less general toxic effects.

Within the last year the substance M. & B. 693 (2-sulphanilyl-aminopyridine) has been produced. This substance has been proved to be particularly effective in dealing with certain types of pneumonia in the human subject.

The work of Evans and Gaisford[4] attracted attention to the value of this preparation. They published the results of treatment of 100 cases of lobar pneumonia with M. & B. 693. The case mortality rate was 8 per cent. as compared with 27 per cent. of a control series observed at the same time. These striking results led to very extensive use of this product, but recently further pharmacological investigation and extended clinical trials have suggested the need for caution in accepting the claims made for this product apart from its established value in pneumonia of one type.

McLean, Rogers and Fleming[5] state that pneumococci have been found to vary enormously in their sensitivity to this drug, and this variation is not associated with the type of pneumococcus, but with the individual strain.

M. & B. 693 has also been shown to be of value in meningococcal and other coccal infections.

It is suggested that M. & B. 693 being more active than proseptasine and soluseptasine, may prove effective in a concentration in the body of less than 1 in 10,000.

Sulphanilamide products have also been found clinically of value in *Brucella abortus* infections in the human.

The difficulty of accurately assessing the value of these drugs in the many conditions in which they have been used has been stressed by many writers to medical journals.

In considering their true value in veterinary medicine, it is necessary to determine whether three requirements have been satisfied :—

Firstly, is the condition for which they are being employed known to be caused by an organism susceptible to the action of sulphanilamide drugs?

Secondly, was the drug employed in a sufficient dose to secure an adequate minimum concentration in the body fluids?

Thirdly, was the frequenty of dosage such that this concentration would be maintained over a period sufficient to allow time for the action of the drug to take place on the organism concerned?

Immediately the second and third requirements are applied, it is necessary to face the question of dosage. If a bovine weighing 6 cwts. was the subject for treatment, it would be necessary to give at least 16·8 grammes (252 grains) every six hours to maintain a concentration of 1 in 10,000. Such dosage if continued for two or three days would prove to be an extremely expensive undertaking. It may be that a lesser concentration is necessary in horses and cattle, but no reliable evidence to this effect is available. Statements have been made that 1 in 40,000 was sufficient for the treatment of certain conditions in cattle, but the results obtained with this concentration when analysed were negative.

In the dog, to obtain a concentration of 1 in 10,000 and maintain it for an adequate period is in many cases an economic possibility.

Toxic Effects.

If the sulphanilamide drugs are to be employed in doses of this magnitude to obtain such concentrations in the body fluids, it is obviously necessary to consider their possible toxic effects.

It is suggested that sulphanilamide interferes with reabsorption of bicarbonate and bases, but no renal damage occurs. A certain degree of acidosis apparently always occurs. More recent reports indicate that the absence of renal damage cannot be entirely taken for granted, and one report referred to five cases of haematuria in human subjects that appeared to be due to the effects of sulphanilamide compounds.

Cyanosis has been frequently observed in the human subject, and it has been stated that a measure of cyanosis was inevitable if the drug was used in the concentration necessary to produce sufficient excretion in the urine to be of value as a urinary antiseptic. I have seen cyanosis in a Scotch terrier following its use as a urinary antiseptic. It was stated that cyanosis was due to the formation of sulphaemoglobin and methaemoglobin, but this has been disproved and cyanosis is now believed to be due to a pigment formed from the particular compound itself.

American writers have described a febrile reaction in cows comparable to a similar reaction seen in the human.

Montgomerie[6] described a tendency towards diarrhoea in cows, and this effect has also been reported in America.

Inco-ordination of gait, difficulty of rising and apparent nervous excitement have also been mentioned by various authors. Toxic symptoms usually clear up on stopping the drug, and I do not know of any death definitely attributed to the effects of sulphanilamide compounds in reasonable doses.

Recently it has been stressed in certain quarters that the toxicity of these drugs has not yet been adequately studied, and that some of the compounds may accumulate in the liver and spleen, causing damage to the former. The possibility of permanent renal damage is not yet entirely excluded.

Veterinary Application.

When the conditions in which sulphanilamide has been used in veterinary practice are studied, there is, as may be expected, some divergence in the opinions expressed as to their value. Montgomerie[6] has reported dramatic recoveries in streptococcal pneumonia in horses, and equally good results have been claimed by other workers, but Fraser[7] stated that prontosil was used without any marked effect. I have found first proseptasine and recently M. & B. 693 of value in bovine pneumonia. This led me to enquire if these substances might be of value in some types of transit fever. The results point to the varying character of the causal organisms of this condition, the only cases appearing to benefit from these drugs being those showing symptoms of broncho-pneumonia. My experience of M. & B. 693 in pneumonia in the dog is as yet too limited to justify any conclusions. Stableforth[8] has pointed out that Group C Streptococci, which are associated with strangles, metritis of mares, possibly joint-ill and some cases of acute bovine mastitis, are susceptible to sulphanilamide treatment in laboratory animals, and therefore in these cases the drugs may possibly be of value. Nairn[9] stated that some cases of joint-ill in foals appeared to respond to sulphanilamide treatment.

At the Royal (Dick) Veterinary College we have been using sulphanilamide in the treatment of purpura haemorrhagica; the results are inconclusive, but merit continuing the investigation.

Stableforth[8] stated that he had not found it possible to carry out experiments in mice regarding the effect of sulphanilamide on Streptococci of Group B which cause ordinary chronic bovine mastitis. I have learnt privately of some work in the use of sulphanilamide in mastitis in which the dose used was so inadequate that any results must have been due to natural recovery. Allot[10] stated that there was no evidence from the tests employed that sulphanilamide produced any permanent destruction of streptococci in the udder.

It is, of course, possible that a sulphanilamide compound may yet be found that will be of value in chronic bovine mastitis.

The successes reported in the treatment of undulant fever in the human being with sulphanilamide suggested that it might prove of value in dealing with bovine contagious abortion. Montgomerie[11] stated that experiments showed that the value of sulphanilamide in the treatment of *Br. abortus* infection of animals merits further investigation.

Mitchell[12] in a paper given to the Scottish Metropolitan Division described a field experiment with results that appear to encourage further investigation using much larger doses of sulphanilamide in the treatment of cows known to be affected with *Br. abortus*. On the other hand, Gordon[13] has stated that he has found no evidence to suggest that massive daily doses of soluseptasine injected subcutaneously over a period of seven days had any effect in reducing the extent of a brucella infection in guinea-pigs.

It is known that neither prontosil nor sulphanilamide has any effect on the virus of canine or feline distemper. Montgomerie and MacIntyre[14] also reported that sodium-sulphanilyl-sulphanilate did not influence the course of infection with distemper virus either in ferrets or in dogs.

Hewetson[15] in describing the use of sodium-sulphanilyl-sulphanilate in an outbreak of distemper-like disease in cats, said that it was difficult to form definite conclusions, but thought benefit was obtained.

It is still very debatable whether sulphanilamides are of any value in the treatment of the complications of distemper.

In two outbreaks of disease in Great Danes, proved to be associated with a beta-haemolytic streptococcus, we found sulphanilamides of no value, but I am convinced that the haemolytic streptococcus was in all probability a secondary invader following a virus infection.

Ullrich[16] stated that prontosil was of no value in canine and feline distemper, but that it was of value in small-animal practice in diseases of the upper respiratory tract, gastro-intestinal tract, wound infection, ascending infection of the urinary tract, and infection of the female genital tract. My colleagues have employed sulphanilamide in post-parturient sepsis in the bitch with some apparent success.

Some encouraging results of the treatment of streptococcal skin conditions in dogs and cats have come to my notice recently.

Ogilvie[17] described a case of pyaemia in a five-months-old bull mastiff. Sulphanilamide was not used until the case was showing signs of

improvement due to localisation of the infection. Sulphanilamide treatment was accompanied with considerable medicinal treatment. It is far from being clear that sulphanilamide had any effect in this case at all.

It seems a reasonable statement of the present position to say that very much more laboratory investigation and field research must be conducted regarding the action of sulphanilamides in diseases of the domestic animals before their value can be sufficiently determined to justify the regular use of them in veterinary practice.

Vitamin D

Standardisation of cod liver oil according to its vitamin content by biological assay is now a recognised practice that should result in the veterinary profession being supplied only with cod liver possessing a stated minimum vitamin content. It should now be possible to state the vitamin requirement for animals in terms of biological units, and it would appear more rational to express our doses for animals in terms of biological units, and not in terms of the volume of cod liver oil.

Preparations of irradiated ergosterol—calciferol and liquor calciferolis—are now included in the British Pharmacopoeia. It has been my experience that these preparations have not given as satisfactory results in the treatment of rickets in the dog as cod liver oil. Similar experiences have been reported in children, and also in a related condition in chickens. It may be that the natural vitamin in cod liver oil is biologically more active than the artificial compound. Halibut liver oil, with its high vitamin content, I have found useful in cases that did not tolerate cod liver oil; the relatively high cost of halibut liver oil precludes its regular use.

Recently it has been suggested that massive doses of high potency vitamin D preparations might be of value where ordinary therapeutic use of vitamin D has apparently failed. Doses for the dog of as much as 300,000 units have been suggested in place of about 3,000 units, which may be regarded as a reasonable dose in cod liver oil for a dog. I have not as yet had an opportunity of utilising this method of massive dosage.

Vitamin A

The value of vitamin A in many respects has been fully appreciated in veterinary practice, but one aspect that does not appear to have received the recognition that it deserved was McCarrison's work on the relation of vitamin A to the formation of urinary calculi.

McCarrison[18] discusses the circumstances under which urinary calculi occur in cattle in India, pointing out that periods of vitamin-want alternate with periods of vitamin-supply, the diet remaining all the while unbalanced with respect to calcium and phosphates. The period of vitamin supply occurs after the rains, which allow the cattle to obtain green fodder. McCarrison was able to reproduce the chemical and physical characters of cattle stone under experimental conditions in albino rats.

"The rats were fed on a diet deficient in vitamin A and containing an excess of lime relative to the amount of phosphate in the diet. By keeping them on this diet for 70 to 80 days, and then supplying the missing vitamin A it was found that of those surviving the process, a high percentage had stones of composition and physical characters closely resembling those of cattle stones. Apparently what happens is this: during the first or vitamin starvation period, an enormous mass of calcium carbonate debris is deposited in the urinary tract. On supplying vitamin A, but allowing the calcium-phosphate imbalance to remain, the whole (if it be small) or part (if it be large) of the calcium carbonate deposited is redissolved and dispersed. But in some cases, parts remain as isolated collections of grains; and during the second period of the experiment, when vitamin A is provided, these act as foreign bodies and a layer or layers of calcium carbonate are deposited around them."

McCarrison said that "the incidence of such stones in rats can be very greatly reduced by adding to the vitamin A-poor and lime-rich diet an amount of sodium phosphate sufficient to form with the excess of lime insoluble calcium phosphate in the bowel. The further addition of vitamin A completely prevents the disease."

This condition of alternate periods of vitamin supply and vitamin starvation must be reproduced on many farms in this country, on which cattle grazing in the summer and housed in the winter receive no fresh food during the winter months. If, in addition, the calcium phosphorus ratio is disturbed on the lines indicated by McCarrison, the conditions are favourable to the production of calculi. My own experience of urinary calculi has tended to support the belief that the principles of McCarrison's work are applicable to cattle in this country. Where the circumstances under which cattle are kept and fed suggest that there is such a lack of vitamin A, it would appear that the addition of cod liver oil to the dietary should prove of considerable value.

Chronic bovine haematuria is a condition that, in my experience, is increasing in certain districts, and also appearing in districts where it had not before occurred. In many cases the methods of husbandry produce periods of alternate vitamin starvation and vitamin supply. It may be that a vitamin A supplement during the winter months might prove of value in preventing the development of these cases, which may quite well develop under conditions of the

urinary mucous membranes such as those described by McCarrison.

Urinary Antiseptics

The introduction of mandelic acid as a urinary antiseptic, particularly for *B. coli* infections, has never attracted much attention, in veterinary medicine; except for small animals, its cost would render it an uneconomic remedy. Nevertheless, the pharmacological principles underlying its use provide certain useful methods that might well be applied in veterinary practice.

The use of mandelic acid as a urinary antiseptic, developed from the observation— frequently made also by veterinarians—that the urine in cases of ketosis does not undergo decomposition in the same way as urine from normal patients. It was then found that the deliberate production of ketosis by means of a ketogenic diet created an antiseptic action in the urine that was of value particularly in *B. coli* infections. A ketogenic diet is an unpleasant one deliberately to adopt for any length of time, and the administration of β. hydroxybutyric acid by mouth is not effective owing to the destruction of that substance in the stomach. Research produced the substance mandelic acid which, when given by mouth, is excreted in the urine, and under favourable conditions as to the *p*H of the urine, acts as an effective urinary antiseptic. Mandelic acid only acts as a urinary antiseptic when the *p*H of the urine is reduced to 5·3 or lower. It can easily be shown that neither this reduction of the *p*H alone nor the mandelic acid alone acts as the antiseptic, but that the combination of the two is necessary. Acid sodium phosphate does not cause sufficient reduction of the *p*H of the urine, and so ammonium chloride is used for this purpose. It is necessary when using mandelic acid to administer with it ammonium chloride and check the reduction of the *p*H by testing the urine with methyl red. Excessive use of ammonium chloride is undesirable, since not only does it produce nausea and sometimes actual vomiting, but if the *p*H is excessively reduced, the risk of damage to the renal tubules becomes considerable. This method of producing urinary antisepsis might be of value in certain canine cases, where the cost of treatment was not a primary consideration. It is interesting to note that some years ago[19] I reported that an alkaline urine was found in the dog in cases of cystitis, the urine from which contained a pure culture of *B. coli*.

It is, however, a development of this method of acidulating the urine that appears to have some veterinary application. In a paper in the *British Journal of Surgery* by Pyrah and Fowweather[20] to which my attention was drawn by my colleague, Professor Mitchell, the aetiology, prevention and treatment of urinary calculi in recumbent patients is discussed. After commenting on the frequency with which urinary calculi develop as a complication of recumbency, these authors discuss the factors associated with their development. They consider that a reduced fluid intake, or excessive loss of fluid, leading to concentration of urine, and a diet resulting in the formation of urine with a relatively high *p*H, are important factors along with a lack of vitamin A in the production of urinary calculi. They have found it possible to prevent the occurrence of calculi by ensuring an adequate daily fluid intake, adjusting the diet in such a way as to give an "acid ash" and providing an adequate supply of vitamin A.

I am indebted to Mr. Nairn, of Blairgowrie[21] for the details of an exceedingly interesting observation made by him regarding the high incidence of urinary calculi in young ram lambs being intensely fed under conditions of close confinement for show and sale purposes. He found that in these cases the losses could be considerably reduced by ensuring that the rams received a reasonable amount of exercise. He also noted that feeding a wet, indeed sloppy, diet in the early period of confinement was of considerable importance. The close parallel between confinement of the rams and recumbency in the human subject is of great interest. The part played by the increased water intake ensured by a wet diet is comparable with the observations made in regard to fluid intake for the human subject.

In the treatment of urinary calculi Pyrah and Fowweather have achieved remarkable success by applying these methods, and in addition, if the *p*H of the urine could not be reduced to between 4·8 and 5·3 by dieting alone, they gave 7 to 10 grains of ammonium chloride in capsules every four hours until the desired *p*H was obtained. They found that in these circumstances the stones disintegrated, for a urinary *p*H of 4·8 to 5·3 is the most favourable for the solution of calcium phosphate. These observations may be of very considerable significance to us in veterinary practice. The dog with recurrent urinary calculi is frequently encountered, and these methods could easily be applied to canine patients. A diet rich in meat gives the necessary "acid ash," vitamin A is easily supplied, and the reduction of the urinary *p*H in the dog with ammonium chloride is perfectly straightforward.

It is also possible to increase the fluid intake of a dog by deliberately administering water to the animal. Some years ago we had in the College a client whose dog had been repeatedly operated on for urethral calculi. This client trained his dog to drink water readily when administered, and in this way was able to keep the animal to a ripe old age.

The reduction of the *p*H of the bovine urine would appear to present more difficulty than that of the canine urine, since the normal *p*H of bovine urine is much higher, being fairly constant in the neighbourhood of 7·8. I have, however, found it possible to reduce the *p*H from 7·8 to 5·0 in two days by means of 2 oz. doses of ammonium chloride given three times daily, lesser doses being required to maintain the *p*H at this low figure. The *p*H returned slowly to the normal figure after dosing with ammonium chloride ceased. There was no disturbance of the cow's general health during the period of this treatment.

This treatment applied to either bulls or bullocks affected with urinary calculi might well prove to be of considerable value in veterinary practice. It would, of course, be necessary to check the reduction of the *p*H of the urine by testing samples of urine with methyl red, and when the desired reduction of the *p*H had been obtained, the dosage with ammonium chloride would require to be reduced to a point where that *p*H was maintained.

Excessive reduction of the urinary *p*H is undesirable, since if maintained for an unduly long period, it may damage the renal tubules leading to the formation of casts.

If in addition to this method of treatment, McCarrison's work as supported by Nairn's observations is applied as a means of prophylaxis, it may be claimed that we now have means at our command of dealing effectively with the problem of urinary calculi in the domestic animals that suffer from this condition.

Summary

The possibility of errors in assessing the value of new discoveries in therapeutic agents is discussed.

The developments in the use of the drugs of the sulphanilamide series are discussed, and the possible explanation of their mode of action detailed. Conditions that should govern the assessment of the value of these drugs in veterinary practice are detailed.

The use of these drugs in veterinary practice up to the present is surveyed and the results analysed.

The need for using only biologically assayed cod liver oil is stressed and the desirability of adopting a dosage for animals based on the biological activity of the oil is advanced.

The association of an absence of vitamin A with the formation of urinary calculi is described.

The pharmacology of mandelic acid as a urinary antiseptic and the relation of its activity to the urinary *p*H is discussed.

The possible value of adjusting the urinary *p*H in treatment of urinary calculi is advanced as being worthy of attention in veterinary medicine.

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The foregoing paper was discussed at the second morning session of the concluding day—Friday, July 28th—of the N.V.M.A. Congress at Great Yarmouth, when Mr. J. H. Poles, M.R.C.V.S., of Whittlesea, presided over a good attendance.

The Chairman at once called upon Dr. A. W. Stableforth, who was the first to open the discussion.

Dr. A. W. Stableforth (Division of Preventive Medicine, Royal Veterinary College), who was the second "opener" of the discussion, said: Before summarising briefly the work which we have carried out in the Division of Preventive Medicine of the Royal Veterinary College on the use of sulphanilamide in animals, there are two comments which I should like to make on the

paper. Whilst summarising adequately the medical point of view Professor Boddie tells us little regarding the general pharmacology of this group of drugs in animals, and I do not think we should assume that animals behave in the same way as human beings; in fact, we have already evidence that animals behave somewhat differently. Professor Boddie also says that the cost of adequate dosage for large animals is prohibitive. I would agree as regards such substances as M & B 693 but not as regards sulphanilamide itself, because, although, as we have shown, large doses are necessary, sulphanilamide is relatively cheap and sufficient to treat a cow or horse for a week can be purchased for about £1. In acute infections a much shorter period of treatment often suffices.

The greater part of our work has been concerned with (1) the tolerance of horses, cows and dogs to sulphanilamide and the dosage required to produce and maintain a satisfactory concentration of the drug in the animal body, blood, milk, etc.; (2) with experiments to find whether certain organisms are susceptible; and (3) with the effect of the drug, when given in what may be regarded as adequate dosage on certain common diseases, including bovine mastitis and abortion, febrile conditions associated with streptococci in horses, such as pneumonia, and certain streptococcus infections in dogs and other animals. Mr. Hignett has been associated with me in all this work and was to have been here to-day to present his work on horses. He has unfortunately been prevented at the last moment and I have the Chairman's permission to give his communication later.

[Dr. Stableforth then described their results briefly, illustrating them by a series of charts to be published with full details later.]

Dosage.—Animals have been given various doses of sulphanilamide, single or repeated, orally or subcutaneously. The toxic effects, if any, were noted and the concentration of sulphanilamide in the blood and milk estimated by chemical methods at intervals afterwards. In horses, cows, dogs and sheep, as in man, sulphanilamide appears in the blood within an hour or two of administration. It reaches a maximum at about five or six hours. Excretion is then rapid; with small doses the concentration is halved in about 12 hours and little is present at 24 hours. With large doses the peak is relatively higher in all species and retention is longer, this being least marked in the dog and most marked in the cow. With small doses dogs appear to show higher concentrations than cows or horses.

Some differences have thus been observed according to species. Certain general figures, although only approximately correct for a given species, may, however, be given. It may be said that after a single small dose per os, *i.e.*, 1 gramme per 20 lb. body weight (86·4 gr. per cwt. or about ¾ gr. per lb.) a peak blood concentration of 5 to 10 mg. per cent. is reached in five to seven hours, higher in dogs than in cows or horses, and that this then falls gradually until at 24 hours little or none remains. After a dose of 1 gramme per 10 lb. body weight (172·8 gr. per cwt. or about 1½ gr. per lb.) a peak blood concentration of 10 to 16 mg. per cent. is reached which falls to about half at 12 hours and to 3 or 4 mg. at 24 hours. After a dose of 1 gramme per 5 lb. body weight (345·6 gr. per cwt. or about 3 gr. per lb.) the peak concentration may reach 30 to 40 mg. per cent., dropping to about two-thirds at 12 hours and to somewhere around 10 mg. at 24 hours, some still being present at 48 hours. Doses of twice or four times this amount produce even higher concentrations but these are unnecessary and attended by undesirable though apparently temporary toxic symptoms.

The sulphanilamide passes in due course into nearly all the tissues of the body and into the milk. It is excreted in the urine. The demonstrable concentration in the tissues is about 60 per cent. of that present in the blood.

We have made a large number of observations on milk samples from cows. The peak concentration in milk is reached an hour or two later than in blood and is usually lower. The concentration is, however, better maintained. After a dose of 1 gramme per 5 lb. body weight, *i.e.*, the largest dose recommended, the milk contains an average of 12 mg. per cent. at 8 hours (120 cows), about 8 mg. at 24 hours (89 cows) and about 2 mg. at 48 hours (50 cows). After a dose of 1 gramme per 10 lb. body weight the values were about 8 mg. at 8 hours and 5 mg. at 24 hours. The concentration reached in the udder of dry cows is lower than that of cows in milk.

Experiments with repeated doses have shown that an adequate concentration, *i.e.*, over 10 mg. per cent., can be maintained in both blood and milk, and presumably in other tissues, by an initial large dose (1 gramme per 5 lb. body weight, 345·6 gr. per cwt. or 3 gr. per lb.), or at least half this dose, followed by subsequent dosing every 8 hours with 1 gramme per 30 lb. body weight (57·6 gr. per cwt. or ½ gr. per lb.). This scheme of dosage will always be meant unless otherwise stated. Experience has shown that if the initial large dose is not given there is considerable delay before the maximum concentration is reached.

Subcutaneous injection has no advantages; in fact, a comparison of similar doses by the oral and subcutaneous routes has shown that the concentrations reached in blood and milk are at each hour lower after subcutaneous administration. Administration by the intravenous route

has the disadvantage that, although it may produce higher immediate concentrations, these soon disappear.

Tolerance.—Large doses of sulphanilamide, twice or four times the highest recommended dose, produce marked inco-ordination of movement or paralysis, inappetence and varying degree of coma, the symptoms appearing within two or three hours and going within six to eight hours. The highest recommended dose (1 gramme per 5 lb.) produces no serious symptoms. It appears to have little effect on dogs. Horses may show some inappetence, sleepiness and perhaps some inco-ordination of the hind limbs. Cows commonly show nothing or only diarrhoea (of variable degree) and some drop in milk yield. They may, however, become sleepy and show some inco-ordination of movement and a definite drop in milk yield. The loss of milk, however, does not average more than 10 per cent. and it may increase. Moderate doses may produce similar but much slighter symptoms. Small doses have little effect even if repeated. They may produce some inappetence after a few days but are tolerated well provided the total dose in 24 hours does not exceed 1 gramme per 10 lb. (say 180 gr. per cwt. or 1½ gr. per lb.) and is not continued beyond seven to ten days.

We have had no deaths in over 200 treated animals and no serious symptoms except in animals which received at least twice the highest recommended dose. One or two unaccountable cases of serious collapse have, however, been reported by others. It is, of course, well known that sulphur-containing substances should not be given during dosage with sulphanilamide.

Therapeutic Use in Animals.—As in man, it appears that sulphanilamide or other members of the sulphonamide group are more likely to be of value in acute conditions, particularly those associated with streptococci. We have, however, also tested them in some of the chronic infections.

Bovine Mastitis.—The effects of the administration of sulphanilamide in bovine mastitis are often remarkable. The clinical symptoms are usually improved and frequently disappear within a day or two and do not reappear for some time. Actual sterilisation of the infection is, however, more difficult. So far we have found that with adequate dosage a little less than 50 per cent. of *Str. agalactiae* infections have been cured. With small doses or doses given at daily intervals the percentage of cures has been much lower.

Bovine Abortion.—Following on Montgomerie's experiments on guinea-pigs and goats we treated some 60 cows with high titres to *Br. abortus* for a period of one week. The result was almost complete failure.

Febrile Conditions in Horses associated with Streptococci.—These have responded very well indeed and will be dealt with in Mr. Hignett's communication.

Dogs.—A small number of cases of streptococcus infection have been treated in conjunction with our clinical colleagues at the College. In general, chronic infections, *e.g.*, of skin, digits or vagina, have failed to respond but a few acute conditions, *e.g.*, a case of streptococcus pneumonia received in an almost moribund condition treated recently, have responded at once.

In conclusion, I would emphasise two points. Firstly, that full co-operation between clinical and laboratory workers is of the utmost importance in order that we may find out the true nature of the condition being or to be treated and thereby be enabled in due course to put on record for our successors data which are adequate from the clinical, pharmacological and bacteriological points of view. Sulphanilamide or other members of the sulphonamide group may otherwise undeservedly fall into disrepute and some of the conditions particularly susceptible never be found. Secondly, that dosage must be adequate, *i.e.*, a large initial dose (1 gramme per 5 lb. body weight, about 360 gr. per cwt. or 3 gr. per lb.)—or at least half this dose—followed by adequate maintenance doses (1 gramme per 30 lb. body weight, about 60 gr. per cwt. or ½ gr. per lb.) at intervals of about eight hours.

Dr. Stableforth now read the following contribution to the discussion forwarded by Mr. S. L. Hignett, B.Sc., M.R.C.V.S., of the Division of Preventive Medicine, Royal Veterinary College, London:—

For some considerable time it has been known that many cases of lobar pneumonia in the horse are associated with a streptococcal infection. In the summer of 1938, W. S. King reported very encouraging results from the use of prontosil in this disease. In November, 1938, he kindly placed at my disposal every case of respiratory trouble occurring in the 3,000 horses in the various studs under his supervision. These cases were particularly valuable because I was given a free hand to take large quantities of blood or other material from the animals if necessary. In addition the commencement of treatment could be delayed if one was desirous of collecting information as to the normal progress of the disease.

In spite of the comparative rarity of equine pneumonia last winter, I was called to 32 cases in all, the temperatures varying from 103° to 106° or over. Fifteen of these cases proved to be typical pneumonia. In each instance the following routine was adopted:—

A clinical examination was made and observations were recorded; about 100 c.c. of blood were taken from the jugular vein (with aseptic

precautions) into a flask containing 900 c.c. of 1 per cent. glucose broth and 0·1 per cent. liquoid (an anti-coagulant which also inhibits leucocytic activity); swabs were taken from each nostril. Cultural examination of the blood revealed the presence of haemolytic streptococci in five cases. From the results obtained in two cases, it is reasonable to assume that had several samples of blood been taken at intervals from all horses suffering from pneumonia, streptococci would have been found in a larger number of these animals. The swabs showed streptococci in very large numbers in all febrile cases, whereas swabs taken from over 300 normal horses disclosed streptococci in only 6 per cent. of the animals and then the organisms were present in only very small numbers.

After blood and swabs had been taken the horse was dosed with sulphanilamide, either in capsule or in a drench. The dose varied from 3 to 6 drachms per cwt. given as a single dose or repeated on two, three or four days. In all cases the temperature was well on the road to normality within eight hours; there was an equally definite, though less rapid, return to normal of pulse and respirations. The convalescent period was shortened to seven days. Unfortunately, time will not allow of a detailed description of each of the above cases.

Following the isolation of large numbers of haemolytic streptococci from subcutaneous oedematous fluid in a case of purpura haemorrhagica in the horse, we have used sulphanilamide in five such cases—four of which recovered fairly rapidly.

[The next opening contribution to the discussion was made by Mrs. M. Sheppard, M.R.C.V.S., of Bayswater, W., but we regret that her observations are not available for publication.—*Editor.*]

The third opener of the discussion was Dr. R. F. Montgomerie, B.Sc., F.R.C.V.S. (Beckenham). In consequence of Dr. Montgomerie's unavoidably early departure from Congress, his contribution was read by Mr. H. E. Bywater, as follows:—

I must apologise for my inability to be present at the session of the Congress which will discuss Professor Boddie's masterly paper. It is most difficult, as third opener of the discussion, to set down beforehand remarks which will keep the sequence of events and not be largely a repetition of what previous speakers have said. One may expect that Dr. Stableforth will draw on his extensive experience of the use of sulphanilamide in animals and cover much of the ground I have in mind. Yet it might well be thought discourteous, since the Provisional Committee have left my name on the list of openers, if I did not offer some small contribution.

That section of Professor Boddie's paper which deals with the sulphanilamide group of drugs is an excellent survey, and I would only attempt to make some comments which may stimulate the discussion and give the writer of the paper further opportunity to enlarge on what he has written.

The desired concentration of sulphanilamide in the treatment of the more acute diseases in the human subject appears to be of the level mentioned, 10 mg. per 100 c.c. of blood; but can one hope to hold it at this concentration in the large animal? In our small experience we have never approached it in cattle when giving sulphanilamide at about the dose rate for that species mentioned in the paper. It has only been reached when the drug was given at or above the rate of 1 gramme per 10 lb. body weight. It certainly appears true that in cattle, as in other animals, the concentration begins to fall soon after the sixth hour, but the loss is not so rapid. Whereas sulphanilamide has disappeared from the blood in the mouse in eight hours and in man in 24 hours, it has not been uncommon in our experience to find it still relatively high 24 hours after dosage in the *cow*—even one-half to one-quarter the maximum concentration. In the milk it may not reach the blood concentration but it is almost as persistent. In cattle practice we have, therefore, tended to accept daily dosage as good practice. Apparently Professor Boddie, employing a smaller dose rate, would insist on administration being repeated at intervals of four to six hours. This point certainly merits further investigation and I think it probable that some intermediate scheme of dosage is nearer the ideal.

It will be generally agreed that single dose treatment with sulphanilamide is, in general, bad practice but we have seen, especially in pneumonia in the horse, dramatic effects follow the first administration. Treatment was continued in some cases only, because we appreciated the danger of relapse when the drug disappears from the body. In this connection one is tempted to speculate whether some of the drugs related to sulphanilamide—some of the sulphones—at present only in experimental use will be found of especial value in animal practice. Although their toxicity is relatively high, their activity is much greater and their slow excretion—perhaps even five times as slow as sulphanilamide—is certainly in their favour.

One has previously heard the plea that one should know the infection with which one is faced before exhibiting sulphanilamide. I would readily agree that the drug must not be regarded as a "cure all" and that in laboratory investigations one should deal with a single and known infection. Surely that rule cannot be applied in the field, and the practitioner faced with a patient whose condition *may* be due to infection with a susceptible bacterium has every justification in prescribing sulphanilamide, pending a

bacteriological diagnosis. Early drug treatment is essential for full success. This point is perhaps particularly well illustrated in joint-ill of foals. We know the variety of organisms which may cause that disease, we know that some are sulphanilamide-sensitive, we may not be able to obtain material suitable for bacteriological diagnosis and we should, I suggest in any case, be perfectly justified in giving treatment with the drug a trial. It may well be agreed that in some conditions, particularly those secondary to virus infections, the bacterial infection is often so mixed that the drug should be tried and treatment commenced as early as possible. Whether there is justification in extending its trial to conditions whose aetiology is as yet unknown, and may not be bacterial, is an entirely different matter.

Professor Boddie has very rightly given the pyridine derivative of sulphanilamide known as M & B 693 some prominence. It has occurred to me that there is some danger that we may bring this valuable preparation into some disrepute in the veterinary world unless we are careful to remember that its *main* claim to fame is its particular value in the treatment of pneumococcal infections and, perhaps, its advantage over sulphanilamide in staphylococcal infections. Are the pneumonias of the veterinary world pneumococcal? Since M & B 693 is much more costly than sulphanilamide, are we justified in exhibiting it outside its special field—present or extended by further work—to its possible detriment?

The paper has made reference to the investigations designed to determine if sulphanilamide is of value in *Br. abortus* infection in animals. Earlier work did suggest that in *Br. abortus* infection in the guinea-pig, dosage at high levels with sulphanilamide was of value. Later observations agree with those of Wilson and Maier that bacteriological cure of *Br. abortus* infection in the guinea-pig only results when the drug is given over a period at a dose rate closely approaching that of the toxic limit. In conjunction with Dr. McEwen we have observed the failure of sulphanilamide in maximum doses to sterilise the *Br. abortus*-infected udder in the several cows treated. The discovery of a drug which bore to *Br. abortus* the relationship which exists between sulphanilamide and certain types of streptococci would be epoch making in the field of veterinary medicine.

In conclusion, I do wish to support Professor Boddie in his plea that, if sulphanilamide is used at all, it be given in doses which have at least some chance of raising, and maintaining, the concentration of the drug in the blood to that level approaching which one may expect it to exhibit any efficiency it possesses. While one certainly cannot say that treatment with sulphanilamide is a perfectly safe procedure, even our heroic dosage has only rarely been attended by other than mild toxic effects which soon subsided when the drug was withdrawn. In large farm animals daily dosage of about 1 gramme per 7 to 10 lb. and in dogs a daily total of about 1 gramme per 5 lb. (in this case certainly divided into two or three doses) would appear in our hands to approach the optimum.

General Discussion

Mr. H. G. Lamont (Stormont, Belfast), said that this was a most important paper and he felt that the Provisional Committee had made a mistake in leaving it until the last day of the Congress. Professor Boddie had done them a real service in preparing this paper, particularly in the form in which he had done it. He would like to make the following comments.

Dr. Stableforth's opening had certainly been very interesting and instructive. In Belfast they (Mr. Lamont and colleagues) had commenced using M & B 693 and as they had been getting good results in certain conditions, they had more or less confined themselves to this particular preparation. As the result of practical experience and before they had carried out blood examinations they had arrived at a system of dosage with fairly big doses comparable to that recommended by Dr. Stableforth. They had been giving two doses in the 24 hours to their pigs. Professor Boddie had made a statement that, "It is most unlikely that one single dose will cure any serious infection." He thought that some of the remarks made by the openers of the discussion would convince Professor Boddie that it was unwise to dogmatise in regard to these preparations. Their own experience in Northern Ireland in the treatment of a condition which they termed "influenzal arthritis," a disease characterised by a very painful arthritis, pronounced lameness and high temperature, and associated with the presence of an organism in the joints apparently identical to the influenza bacillus, indicated that one dose of "693" had often most spectacular results. The dose they used was approximately 0·75 gramme per lb. body weight. This dose had been given to pigs which from previous experience of the disease they knew would have died in about 36 hours. Instead, at the end of that period, one could not have identified the affected pig from its fellows, recovery had been so quick and so complete. Pneumonia was a serious and common condition in pigs. Clinically they had had very encouraging results from the use of "693," and again the results appeared to be better when they had given two large doses, the two doses combined corresponding to 1 gramme per 10 lb. body weight in the 24 hours, and desisting from further dosing for several days. In a great many cases recovery had followed without subsequent dosing. In passing it might be noted that pneumonia in pigs was not associated with pneumococci.

Their attention had been drawn to the fact that following dosing with "693" pigs often passed worms. A similar occurrence in dogs had been noticed by Mr. Ritchie in Belfast. In one or two instances blood had been noticed in the urine of pigs following dosing with "693." This had not appeared to have any serious effect and had been mentioned by the attendant casually.

About a year ago an article on the use of

oestradiol benzoate (Di-men-formon) as an agent for the induction of oestrum in ewes had appeared in the *Veterinary Journal*. They had used this preparation with very good results in sows.

They had also used nembutal as an anaesthetic in pigs, and later soneryl sodium. With this latter preparation they had noticed the absence of muscular twitchings.

Dr. W. P. Blount observed that he would like to say, with reference to the continuous dosing of sulphonamide to cattle, that he thought that it was quite correct to suggest that it should not be given for more than ten days; they had had definite toxic symptoms—he was speaking now of Jersey cattle. Some cows had shown symptoms after having received only 250 tablets; others had gone on to 1,200 tablets before showing typical symptoms—loss of balance, loss of appetite, etc.

He thought Professor Boddie was wrong, however, in suggesting that they should know whether an organism was susceptible to the action of the drug before administering it; if they stuck to that they would not get very far. Cyanosis they had not observed, nor diarrhoea, but inco-ordination of gait was very marked.

In his experience sulphonamide had been successful in streptococcus mastitis of cattle.

With reference to vitamin D, would Professor Boddie disagree with a standard of 1,000 A and 100 D International Units?

They had found that rickets in chickens could be cured easily by using other fish liver oils than cod. Was there not an error in the standard dosage of 3,000 units for dogs; should it not be 300 units?

He was glad that mention had been made of cod liver oil and chronic ulcers: was there any evidence that the effect was increased with an increased vitamin content of the oil?

Had Professor Boddie had any experience of prominal, which was a new drug used very successfully in epilepsy in man, and which had perhaps an application to hysteria in dogs?

Mr. H. W. Steele-Bodger stated that, with reference to what had been said about nembutal anaesthesia and pentothal sodium, he would like to record that they had used these two drugs in conjunction in cases which they knew to be fairly septic, such as cases of chronic metritis where one had a uterus full of pus. It was safer, he thought, and a little longer in effect than the pentothal sodium injection to use nembutal with it.

With regard to prontosil, he would like to give one word of warning concerning its use in cats. They had had three unhappy experiences. They had given it to three cats which were not seriously ill, but which had chronic suppurative conditions; they all died within two or three hours and none of them had had any other form of drug treatment. In dogs they had found that prontosil had an aperient action which continued for several days and occasionally produced a "paddling" action in dogs not unlike that of a cow with milk fever.

In cases of husk-pneumonia in heifers, sulphonamide was very valuable indeed.

The Reply

Professor G. F. Boddie said that, first of all, if they would allow him he would say that after serving on two provisional committees and attending a number of Congresses, he was convinced that it was a very wrong policy to have two papers to discuss on the Friday morning: it was not fair either to the essayist or to the openers or to the general body of members who wished to give more time to the discussion of the paper than was available under such circumstances. (Hear, hear.)

He thought the best way to answer that discussion would be to take each speaker in turn and deal with the points he had raised. Dr. Stableforth had kindly supplied them with a most valuable sequence of data regarding the use of sulphonamide and those charts, if published in the *Veterinary Record*, as he suggested they should be, would be of very considerable value to those of them who were trying to use that drug in practice. It seemed to him, however, in studying those charts, that it was quite probable that some of the statements he (Professor Boddie) had made about the frequency of dosage might have to be amended although he did not think that the general terms of the postulates he laid down on page 4 of his paper had been seriously challenged.

Dr. Stableforth's results in getting 47·8 per cent. of cures of mastitis were tremendously encouraging evidence and he wished him all success in that field: it might be that some other allied compound would be even more successful, or that might be achieved by adjusting the dosage.

It was rather typical of the position in regard to sulphanilamide that Dr. Montgomerie should report failure in the treatment of mastitis; so even that day they had got a contradiction of opinion amongst equally competent observers. There seemed to be a fair consensus of opinion that so far sulphanilamide was not of much value in contagious abortion in animals. The observations of Dr. Stableforth and Mr. Hignett were very interesting and suggested a promising field in horse practice for the use of products of the sulphonamide group.

Mrs. Sheppard began by agreeing with him to a very large extent and then started to take him to task in regard to certain omissions: he did feel that some of her remarks in that respect were, perhaps, a little bit unreasonable, because if he had included all the things that it was suggested to him by her that he should have included, it would not have been a paper he would have written—it would have been an encyclopaedia of about 1,000 pages. One must deal more or less adequately with the few agents one had the space to select and not merely make a catalogue. In any case he could not agree that the barbiturate group of drugs was a recent advance: none of them was in any doubt as to their value. Dr. Blount was, apparently, some 15 years behind the times when he asked him if he had heard of prominal—he had heard of it and had prescribed it some years ago; it was a useful drug in some respects but for the tendency it had to put the dog off its legs. There were, of course, better British equivalents.

Dr. Montgomerie had given them some interesting details regarding blood concentrations and the dosage that he found necessary to achieve, not the concentration he (Professor Boddie) indicated in the paper, but the concentration which he found gave effects. That, perhaps, was the point which he thought he had summed up on page 5 when he said, "It seems a reasonable statement of the present position to say that very

much more laboratory investigation and field research must be conducted regarding the action of sulphanilamides in diseases of the domestic animals before their value can be sufficiently determined to justify the regular use of them in veterinary practice."

He was particularly glad to hear Mr. Lamont's contribution because at the time he wrote the paper he was not in a position to say anything regarding the use of sulphanilamide in pig diseases and he did not know that in Northern Ireland they were using these drugs with some success; he thought very probably there was quite a big field for their use, particularly in regard to some of the diseases that played havoc with young pigs.

He had had some correspondence with May & Baker about "693" and they had given him details of the results of using that drug in big pedigree herds, which results had been of considerable value. He was struck with Mr. Lamont's observation that "693" would produce haematuria in young pigs. In America there was a considerable volume of feeling that the toxicity of these drugs would require them to be much more thoroughly explored: he was not at all sure that one reason why he was not at last year's Congress was the effect of sulphanilamide rather than the disease for which it was prescribed. (Laughter.)

He was sorry that reference had been made to the use of "693" as an anthelmintic as it would encourage its indiscriminate use still more.

With regard to the treatment of mastitis with sulphanilamide, one man's method was to give the cow one pound of this agent and the animal apparently suffered no ill effects.

Dr. Blount disagreed with the postulates he laid down on page 4 of his paper; he thought that anybody who laid down postulates must expect somebody to disagree with them and he (Professor Boddie) did not think he had said anything that interfered with them seriously.

He had not used lentin at all extensively and that referred to some of the things mentioned by Mrs. Sheppard.

Mr. Steele-Bodger's remarks in regard to the combination of the two drugs, nembutal and pentothal sodium, were interesting, but he thought the most valuable part of his observations was his suggestion that sulphanilamide might be of some use in the treatment of husk; if that really proved to be the case he thought they would have made a considerable advance.

The Chairman expressed the thanks of the audience to Professor Boddie for his excellent paper and informative reply.

WAR RISKS PERSONAL ACCIDENT INSURANCE

In a recent issue we drew attention to the "Air Raid Precautionary Accident Insurance Scheme" formulated by the A.R.P. Insurance Association, 3, Bucklersbury, London, E.C.4, providing cover at normal rates in spite of the exposure risk inseparable from the carrying out of veterinarians' duties in war-time. In this connection we learn that a special rate of premium is quoted for members residing in non-hazardous districts, who should send in a proposal form for quotation purposes only, when each case will be considered on its merits with regard to geographical situation, etc.

The Veterinary Record

October 14th, 1939.

Recent Advances in Therapeutic Agents for Veterinary Use

RECENT advance in the subject of therapeutic agents is necessarily of great interest to those of our readers who are in practice and it was unfortunate therefore that the discussion on Professor Boddie's paper had to be considerably curtailed. Professor Boddie wisely chose to confine his attention to a few of the more important advances, namely, the sulphonamide group, vitamin D, vitamin A, and urinary antiseptics, rather than to deal cursorily with a larger number of substances. There was little discussion on the last three of his subjects and we may assume, therefore, that his presentation of these was acceptable to the members present. We would commend them to all our readers.

The essayist's survey of the results obtained in humans with members of the sulphonamide group and of the rather meagre data so far published regarding animals, supplemented by his own observations, formed the basis of most of the discussion. The question of dosage deservedly received some prominence, more especially with contributions of Drs. Montgomery and Stableforth, the latter showing charts indicating the dosage of sulphanilamide itself required to produce what may be regarded as adequate concentrations in blood, milk and the body fluids in general. It appears that approximately 1 gramme (15½ gr.) per 10 lb. body weight—180 gr. per cwt.—is required as a first dose (double this dose can safely be given) and that subsequent doses of one third this amount should be given at intervals of eight hours; though with cattle a single large daily dose may suffice. Some inappetence, inco-ordination of movement and, in cows, diarrhoea and some drop in milk yield may follow large doses, but it is generally agreed that these effects are temporary and that no serious toxic symptoms are to be expected, provided that sulphur-containing substances are not given at or about the same time. It is not yet certain that there are no delayed toxic effects, *e.g.*, on liver, spleen, blood, but so far no evidence of these has

appeared in animals. Regarding other members of this group it may be said that, whilst less is known, it may be presumed, pending further data, that dosage for animals should be proportionately large.

We have yet far to go before the range of clinical or bacteriological entities susceptible to members of this group is known. Nevertheless, there is already, as the discussion at the Congress showed, a considerable body of evidence that substances of this group—and so far as we yet know sulphanilamide will do nearly all, if not all, that any other substance of the group will do—are of outstanding value in certain animal conditions, notably, pneumonia and associated febrile conditions in horses, bovine mastitis (certainly from the point of view of clearing up clinical symptoms), joint-ill in lambs and certain febrile conditions in pigs and dogs. It is agreed, on the other hand, that amongst other conditions they are of no value in bovine contagious abortion and in staphylococcus infections.

We have now in our hands a substance, or group of substances, which seem destined to relieve economic loss and animal suffering in a striking manner. It is easy to be dazzled and the more important is it, therefore, that our appreciation should be marked by a decision to use one and all with due discretion and an eye to the accumulation of a body of data which in a few years' time will tell us when and where they are of value. It would be unreasonable to suggest that they should not be given until a bacteriological or other examination had shown that the condition at hand was associated with an organism known to be susceptible. But it is not too much to ask—aware though we are of the calls on our readers' time—that careful records should be kept, dosage be adequate and reasonably constant, and every endeavour made to arrive at a bacteriological, as well as a clinical, diagnosis by submission of all possible material, blood, pus, milk, etc., to a laboratory interested or co-operating in the work. The value of such co-operation is self evident and many of our more striking advances in other fields have followed such co-operation. Let us take a long view and whilst pressing for actual experimental observations, make full use of our opportunities in practice to enlarge the common fund of our knowledge. In conclusion may we remind ourselves that, whilst accurate and recorded clinical observation and experiment must both play their part, the former has—more often than is apparent at first sight—led the way to the solution of our problems.

ABSTRACTS

[Pathogenicity of Trichomonas in Cattle. Beller, K., Schaaf, J., and Scherle, H. (1938.) *Arch. Tierheilk.* **73.** 171-187.]

This interesting paper begins with a brief review of the literature.

Pure cultures only of *Trichomonas foetus* were used, derived from two cases of pyometra; these were freshly obtained so that their virulence was not reduced by repeated passage through cultures.

One young bull and nine young cows were used, all of which were clinically free from disease of the sex organs, serologically negative to Bang infection and repeatedly shown by microscopic examination and by culture to be free from *Trichomonas foetus*. The bull had never been used for service and the cows had not been served and were therefore very susceptible to trichomoniasis. The authors' failure to find *Trichomonas foetus* in these uncovered animals is, they say, in contrast to the reports of some other workers. Calcium and phosphorus salts were given to avoid mineral deficiency and great care was taken against possible secondary infection.

The bull was successfully infected by repeated injections of *Trichomonas foetus* into the foreskin and rubbing it into the folds of the penile mucosa and also by letting it serve healthy cows infected vaginally by pure cultures of *Trichomonas*. Its sexual desire and capacity to serve were not unfavourably affected.

Detection of *Trichomonas* in the bull by culture and microscopical examination was uncertain; its presence can often only be proved by service of a healthy cow.

Intravaginal infection of cows with pure cultures of *Trichomonas foetus* resulted in infection of the uterus even when *Trichomonas* was not demonstrable in the vaginal secretion.

Trichomonas can infect the pregnant uterus without causing any constant microscopic changes in the foetus or its membranes, but, if the infection progresses, the foetus and its membranes and the amniotic and allantoic fluids are also infected.

The pathogenic action of *Trichomonas foetus* was not constant, especially when older cultures were used, although the organisms often settled in the sex canal.

Pregnancy can develop in spite of an existing infection, *i.e.*, "self cure" can occur.

"Vesicular vaginitis" (*Bläschenausschlag*) arising with a *Trichomonas* infection, does not favour the latter, but the two occur naturally together.

The authors could not exclude constitutional differences between the individual animals used and recognise that, with other animals, the

same experiments might give different results. They state that it is impossible to say how far a fundamental organic weakness of the uterus or a high virulence of the Trichomonads may contribute to an infection. There is a brief bibliography.

G. L.

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[Pasture Hygiene with respect to Parasitic Diseases. Mönnig, H. O., and Taylor, E. L. (1938.) Papers to Thirteenth Int. Vet. Cong.]

Mönnig discusses the factors influencing infection with parasites acquired at pasture and he emphasises that percutaneous infections (as with *Gaigeria* or *Bunostomum*) are independent of pasture hygiene and occur mainly in moist stables or around watering places. Apart from mineral deficiencies in the vegetation, the type of soil plays an important rôle particularly as regards texture; thus sandy soil is more favourable for the development and persistence of nematode larvae than a finer clay soil. The type of vegetation and its abundance is also important as intensity of infection is often proportional to the density of cover produced by the different types of grass; where animals have to graze close to the ground heavier infections are acquired. The interval between successive grazings is also important although the length of life of parasitic nematode larvae depends greatly on moisture, temperature and shade. The question of residual infection in a pasture renders control of some genera of parasites particularly difficult; for instance, *Ostertagia* and *Nematodirus* may perisist in sufficient numbers for eight to ten months to produce severe infections, and fully developed eggs of *Trichostrongylus* spp. can resist desiccation for 15 months or longer.

Taylor discusses the subject in rather more detail than the previous author and emphasises that the helminthiases of grazing animals are man-made diseases for the control of which knowledge of the biology of the larvae is important. It is stated that sheep suffering from trichostrongylosis may pass from 9 to 30-odd million trichostrongylid eggs per day and healthy horses from 1½ million redworm eggs daily, diseased horses passing from 30 to 50-odd million or more. As the larvae developing from these eggs are extremely resistant an immense accumulation of viable infective larvae occurs while a pasture is occupied.

Information is needed not only of the longevity of larvae but also of the rate of their death in pastures. For example, it has been found by Taylor that death of some of the strongylid and trichostrongylid larvae begins almost as soon as the infective stage is reached and the diminution of infective larvae proceeds at a more or less constant and rather rapid rate for four or five months, by which time 75 per cent. of the larvae on the herbage are dead; the rate of mortality then becomes slower and the remaining quarter of the larvae does not disappear for another three or four months. *Strongylus* larvae appear to persist longer than *Trichonema* or *Trichostrongylus*.

Taylor has already shown that the increase of infestation in a pasture increases as the square of the number of animals there grazing. By evolving a technique for estimating the number of infective larvae per pound of herbage Taylor has ascertained that an average sheep pasture carries about 200 infective larvae per pound of herbage, a heavily infected pasture up to 500 per lb. and where acute parasitic gastritis is occurring, from 1,000 to 2,500. His observations on horse pastures show that in well-managed thoroughbred paddocks from which faeces were collected daily there were less than ten larvae per lb., whereas a small field used for grazing army horses carried 5,600 and a paddock used for visiting mares at a public stud carried 6,800 per lb. of herbage.

Among the factors influencing the increase of larvae in pastures it is stated that during prolonged periods of extremely dry summer weather there is, on drier pastures at least, a complete cessation of the development of larvae to the infective stage, and even heavy dew does not seem to provide sufficient moisture to allow development. In spite of this, however, an accumulation of the drought-resisting embryonated eggs of *Trichostrongylus axei* may occur and on return of damp weather their development may be resumed. There, then, may be danger of a mass development of infective larvae with occurrence of parasitic gastritis in the sheep. If, however, the drought is followed by slight rain the eggs may be induced to hatch and the less resistant first- and second-stage larvae which emerge may be destroyed by subsequent desiccation.

The amount of herbage is very important; where the grazing is close the intake of larvae is greatly increased. Taylor also finds that a larger number of larvae are acquired from clover than grass as the larvae tend to congregate higher up on the clover plant, on the trifoliate lamella, whilst on grass they tend to remain on the under side of the lower leaves. It is suggested that this may account for the increase of parasitic gastritis following the use of basic slag with its resultant increase of wild white clover in the pasture. It was also found that whereas grass carried 1,900 larvae per lb. adjacent sainfoin carried only 550 per lb., presumably on account of the very slight contact that the large sainfoin plant makes with the ground. The trampling of faeces into the soil, as where sheep are closely penned, results in a marked increase of larvae which

develop to infectivity. (In a laboratory experiment Taylor found that 25 times as many larvae developed when infected faeces were poked into the soil as when left on the surface.) Although the application of farmyard manure to pasture increases the store of infective larvae it may be of less importance than supposed since conditions in the heap are unfavourable for larval development. Removal of the outer five or six inches of the heap is a precaution recommended.

Among the factors influencing the disappearance of infective larvae from pastures time is one of the most important, for, as already stated above, disappearance begins almost as soon as the infective stage is reached. Considerable benefit is, therefore, to be derived from adequate resting of pastures. Grazing by unsuitable host animals is perhaps the most efficacious method of reducing the infective larvae as larvae finding an unnatural host are destroyed; for instance, each sheep placed on a horse pasture containing 6,000 redworm larvae per lb. of herbage would pick up and destroy some 90,000 larvae daily.

Other factors causing varying destruction or removal of larvae include manuring with nitrates (the number of larvae per lb. is reduced by the rapid growth produced), haymaking, the burning of rough pastures, ploughing and harrowing.

The application of artificial manures and other substances for the destruction of larvae is not yet thoroughly efficacious or practical, for destruction of larvae involves more or less destruction of herbage.

Sea water, when applied liberally, as by flooding, destroys strongylid and trichostrongylid larvae, cercariae of *Fasciola* and slugs and snails carrying lungworm larvae, but also damages the herbage, as also does an adequate dressing of common salt. Dressings of Kainit and calcium cyanamide have the most effect but their uses are strictly limited. Copper sulphate can, however, be effectively used for the destruction of the intermediate host snails, and substances lethal to earthworms may be used for the control of lungworms in sheep and pigs, gapeworms and some tapeworms of poultry and pheasants.

J. S. S.

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[Immunisation of Birds against Fowl Pox and Pigeon Pox respectively with Viruses propagated on the Chorio-allantoic Membrane of the Developing Egg. Glover, R. E. (1939.) *J. comp. Path.* **52.** 29-46.]

The present methods of immunising poultry against fowl pox are not completely satisfactory as regards duration and strength. The experiments recorded by the author had the object of investigating the possible value of fowl and pigeon strains as immunising agents after cultivation on the chorio-allantoic membrane of the developing egg. One of the advantages of such a method of virus propagation is that bacteria-free suspensions can be obtained suitable for parenteral inoculation; it was hoped that some beneficial change might occur in the nature of the virus strains as regards virulence and immunising properties.

A fowl pox strain has been carried through 38 generations and at this stage showed some loss of virulence but was still capable of producing generalised disease. A pigeon pox strain after 50 generations showed decreased virulence for the pigeon but produced slightly more severe local reactions in the fowl without causing generalised lesions.

As regards immunising properties a single intradermal dose of the egg membrane virus resulted in considerable protection but no more than that produced by the natural virus; this protection could, however, be increased by a parenteral injection about a month later. The degree of immunity established was tested by inoculation of graded doses of virus; the response to contact infection was not examined at this stage.

W. M. H.

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[Ascorbic Acid Content of Liver and Adrenals of Some Domestic Animals. Weitzenberg, R. (1939.) *Arch. Tierheilk.* **74.** 228-232.]

The ascorbic acid content of the liver and the adrenals of cattle, pigs, sheep and horses was estimated by the methylene blue method of Martini and Bousigore. The content was much the same in all animals examined, being 20 to 25 mg. per cent. in liver and 150 to 170 mg. per cent. in the adrenals. No difference between the summer and winter values was found. Cattle suffering from tuberculosis had a lower amount of ascorbic acid in the liver than healthy animals. The smallest amount was found in the livers of animals suffering from inflammatory diseases such as pneumonia, endometritis, etc.

J. A. N.

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[Use of Cod Liver Oil and Raw Liver in Veterinary Practice. Hegyeli, Z. (1939.) *Arch. Tierheilk.* **74.** 216-227.]

This is a clinical article in which the author describes the successful treatment of a variety of conditions in young pigs by the injection of cod liver oil and the feeding of raw pig liver.

A first injection of 10 c.c. of cod liver oil is given intravenously, followed at intervals of seven to ten days by subcutaneous injections of 9, 7 and 5 c.c. At the same time the raw liver is given at the rate of 3 lb. per day for the first week, increasing to 6 lb. the second week when it can be mixed with a little maize or barley

meal. It was found that if liver was fed for longer than eight weeks at the above rate a condition of catarrhal enteritis developed.

Unthrifty pigs suffering from no definite ailment, pigs affected with pneumonia either parasitic or bacterial in origin and others with symptoms of indigestion or anaemia, have returned to normal weight and bloom after treatment. N. S. B.

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[On the Action of Hypodermatotoxin upon the Germinal Cells of the Experimental Animal. I.—On the Occurrence of Abnormal Gall Bladder among Offspring of Male Rabbits treated with Hypodermatotoxin. Ono, S. (1937.) *J. Jap. Soc. Vet. Sci.* **16.** 51-52.]

When normal female rabbits were served by males which had received injections of hypodermatotoxin over long periods (68 to 135 days, total amounts of toxin 75 to 195 c.c.), 28 per cent. of the resulting progeny were found to have abnormal gall bladders. When females which had received similar doses of the toxin were bred to normal males there was no abnormality amongst the offspring. Repeated injection of the toxin into females during the first 24 hours after breeding to normal males resulted in only one abnormal gall bladder. When both males and females were treated with toxin and later bred, the gall bladders of the progeny were normal. In the abnormal cases the gall bladder was either absent or rudimentary. In explanation it is assumed that hypodermatotoxin in some way causes changes in the spermatozoa of treated rabbits which subsequently affect the development of the mother cell of the gall bladder in the fertilised egg. N. J. S.

SCOTLAND'S POULTRY STOCKS

The decline in Scotland's poultry stocks which set in during 1936-37 is shown by official figures to have been common to practically all counties. Only two counties stood out as exceptions. These were Orkney and Shetland, a tribute to the health of the stock reared in these sea-girt parts. Aberdeen still stands as the county with easily the largest poultry stocks—1,374,373 head of fowls out of Scotland's total in 1937 of 7,197,319. Ayr is second with fully 770,000 head of fowls, and Orkney, small as it is, comes third with 517,137. Though stocks of all poultry declined by 9·5 per cent. on the 1936 figures the total output of eggs and poultry in that year in Scotland is estimated at £3,190,000, which is 7·7 per cent. of the general farming output of £41,345,000, and is practically equal to the combined value of our grain crops. The estimated gross production of hen eggs is put in 1937 at 455 millions, and of duck eggs 13·9 millions. The most striking way of studying the Scottish poultry position is to take the number of fowls per 1,000 acres of land under crops and grass. In this test Orkney is quite outstanding with 4,749 fowls per 1,000 acres against Aberdeen's 3,223, Ayr's 2,552, Dumbarton's 2,506, and Shetland's 2,556.—*Farming News.*

REPORT

[Punjab: Report of the Civil Veterinary Department for the Year 1937-38. [U. W. F. Walker] (High Commissioner for India, Aldwych, W.C.2. 5d.).]

The Government of the Punjab has placed on record in feeling terms the great loss the Department suffered from the death of Mr. T. F. Quirke, the late Director. It is stated that under his expert guidance the Department achieved a position not excelled by that of the Veterinary Department of any other province in India. Captain U. W. F. Walker has been appointed to succeed him.

The report is an interesting record of progress and efficiency. There are seven photographs, including one of Mr. Quirke.

The superior staff consisted of a director of veterinary services, five superintendents, eleven deputy superintendents and one veterinary investigation officer for district work; one superintendent, two assistant superintendents and two deputy superintendents employed at the Government Cattle Farm, and the Principal, seven professors, a hospital surgeon and four assistants at the veterinary college. The post of an additional deputy superintendent remained unfilled.

The subordinate staff employed during the year was 405.

Breeding Operations.—For the second year in succession the Government Cattle Farm at Hissar suffered from a season of drought and a grave depletion of the fodder reserve caused great anxiety. In spite of this the livestock increased in number from 9,324 animals to 9,882. For breeding purposes 987 animals were issued, including 507 pedigree bulls and 204 approved bulls. In addition 1,724 animals, against 1,429 in the previous year, were issued for breeding and draught purposes. There is a very keen demand especially for pedigree bulls.

Progress is reported in the milk yield of the cows on the Farm, and valuable work is being done in connection with sheep and goat breeding. Successful progress was made in the districts in cattle breeding, buffalo breeding, horse breeding, camel breeding and sheep and goat breeding. The number of cattle fairs increased.

Disease. — Rinderpest and haemorrhagic septicaemia continued to claim the greatest percentage of mortality in cattle and there was a slight increase on the figures for the previous year. Preventive inoculation was carried out on a large scale: 805,034 head of cattle were vaccinated against rinderpest with goat virus tissue vaccine compared with 69,116 in the previous year, and, in addition, a large number of inoculations and vaccinations were carried

out against haemorrhagic septicaemia and black-quarter. Thirty cases of glanders were detected and destroyed. Outbreaks of surra were more numerous than usual; 3,908 cases were treated at 50 centres.

Four new hospitals were opened during the year, making a total of 304. In addition, 1,216 outlying dispensaries were maintained. The total number of patients treated in the veterinary hospitals was 1,704,578.

Veterinary College.—The popularity of the college was well maintained; 228 candidates applied for admission against 87 vacancies.

The college hospital was busier than ever, the average daily attendance of patients rising from 173 to 214. Valuable research work was done at the college during the year and Chandhri Mustaq Ahmad, the hospital surgeon, was awarded a gold medal by the All-India Veterinary Association in appreciation of useful veterinary instruments invented by him.

General.—The report is full of interesting detail and the Government of the Punjab is satisfied that steady progress has been made in every direction.

It is recorded that the high standard of work is reflected in the various prizes and medals won by different Punjab breeds of cattle at the All-India Cattle Show at Delhi.

G. K. W.

In Parliament

Poultry Bill Withdrawn

It was expected that the long-awaited Poultry Industry Bill would be passed through this session: the war-time emergency, however, has cancelled all hopes of this speedy passage. The Poultry Industry Bill has been withdrawn in the House of Commons, although it had gone through all its stages in the House of Lords, where it was introduced with great optimism.

This means that the Bill will have to start all over again when the war is concluded. Meanwhile, legislation dealing with the poultry industry will be concerned only with emergency proposals. The poultry industry will therefore take its place unconditionally in the general plan.

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The following questions and answers have been recorded in the House of Commons recently:—

Remounts (Price)

Brigadier-General Sir Ernest Makins asked the Secretary of State for War whether there is any fixed maximum limit for the purchase of Army remounts; whether he can state the reason; and whether a similar limitation exists in respect of any other property or commodities which the War Office is commandeering at the present moment for various purposes?

Sir V. Warrender: The instructions to impressment officers prescribe a maximum price for horses, based on the prices at which the type required for Army service is normally obtainable. Owners who are not satisfied that the price tendered represents fair market value have the right to appeal to a county court judge. The instructions that have been issued regarding requisitioning generally are designed to secure that unduly expensive property shall, so far as possible, be avoided.

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Milk

Mr. David Adams asked the Minister of Agriculture whether he is aware that under the Milk (Special Designations) Order, 1936, samples of milk collected and submitted by the Newcastle-upon-Tyne Corporation to the bacteriolgist for examination, still show many unsatisfactory results; and what steps are being taken to protect the public against this contaminated food, and particularly for an improvement in the low-wage standards of many farm-workers employed in this industry which would conduce to this end?

Sir R. Dorman-Smith: My right hon. Friend the Minister of Health is in communication with the corporation with regard to the first part of the question. As regards the latter part I would refer the hon. Member to the answer which I gave to his written question on September 27th.

Brigadier-General Clifton Brown asked the Minister of Agriculture whether the war will affect the grants made under the attested, tuberculin-tested and accredited herds schemes; or whether the present extra bonus will continue to be paid by the Milk Marketing Board for these categories of milk as heretofore?

Sir R. Dorman-Smith: The Milk Industry Act, 1939, which provides for the payment of quality premiums in respect of tuberculin-tested and accredited milk and milk from attested herds, remains in force and the premiums will accordingly continue to be paid for those categories of milk by the Milk Marketing Board. The premiums are independent of the bonus payable under the Tuberculosis (Attested Herds) Scheme.

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Meat Control

Mr. Henderson Stewart asked the Chancellor of the Duchy of Lancaster why it has been decided to close down local abattoirs and centralise the slaughter of meat in a few centres many of which are unsuitably placed; if he is aware that this change will cause inconvenience to thousands of towns, waste of time and of petrol and add greatly to the expenses of butchers, and thus raise prices of beef to consumers; and whether he will delay execution of this scheme until the necessity for it has been established and the details of the plans approved by those likely to be affected by it?

Mr. W. S. Morrison: The details of the Meat Control Scheme which it will be necessary to put into operation as part of the rationing arrangements have not yet been finally settled. I cannot, however, accept the implications in the second part of my hon. Friend's question. I have already stated that control schemes will not be put into operation until consultation has taken place with the interests concerned. This

applies to the Meat Control Scheme, but I cannot undertake to delay its operation until there is universal agreement.

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Cod Liver Oil

Sir A. Baillie asked the Chancellor of the Duchy of Lancaster whether he can make any statement as to the shortage of cod liver oil, which is vital for modern rearing of young chickens; and whether steps are being taken to provide increased supplies?

Mr. W. S. Morrison: I am not aware of any shortage of cod liver oil. I am, however, looking into the question of future supplies and will bear in mind the point raised by my hon. Friend.

Notes and News

The Editor will be glad to receive items of professional interest for inclusion in these columns.

Diary of Events

Oct. 23rd.—Meeting of the Editorial Committee, N.V.M.A., at 36, Gordon Square, W.C.1, 4 p.m.

Nov. 1st.—All changes of address to be reported to Registrar, R.C.V.S.

Nov. 9th.—Commencing date of Animal Management Examination.

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STUDENTS WHO HAVE BEEN CALLED UP

In view of the fact that veterinary students who have passed their second professional examination are now qualified to be reserved occupationally at all ages, the following instructions are published:—

(1) Students who have passed their second examination and who have already undertaken military service will not be released automatically from any service obligations they may have incurred. Those who wish should apply through the Royal College of Veterinary Surgeons to the War Office for release from their obligations in order to continue their studies. Cases will be dealt with sympathetically.

(2) Any such student will presumably not be called up for future service. If such a student has been registered, application for his release should be made by the student through the Principal of the College to the Secretary of the Royal College of Veterinary Surgeons, who will transmit the application to the Ministry of Labour.

(3) Applications for postponement of calling up in the case of a student who is about to sit for an examination should be made to the Ministry of Labour direct and a copy of the application should be sent to the Secretary of the R.C.V.S.

N.A.R.P.A.C. SMALL-ANIMAL REGISTRATION SCHEME

The National A.R.P. Animals Committee has undertaken the task of registering the small animals of Britain in order to facilitate the restoration to their owners of terrified strays, of which it is likely that, after an air raid, there will be a large number, as animals are not allowed in public air raid shelters and the police, with their other heavy duties, may find it difficult to deal with them. This registration will make necessary the enrolment of a great army of voluntary national animal guards, who will visit all animal owners and will invite them to attach an identity disc to each of their animals. A call is made for volunteers, who are asked to communicate with the N.A.R.P.A.C. National Registration Department, 166, Cromwell Road, S.W.5.

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PERSONAL

Forthcoming Marriage. — Taylor—Hannam.—The engagement is announced between Douglas William Bulpin, youngest son of Mr. and Mrs. R. B. Taylor, of Hendford Lodge, Yeovil, Somerset, and Lilian Mary (Pat), youngest daughter of Mr. and Mrs. S. C. Hannam, of Kings Green, Bourbon, Dorset.

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R.C.V.S. OBITUARY

Hamilton, James R. R., East London, Union of South Africa. Graduated N. Edinburgh, December 19th, 1894. Died July 31st, 1939.

Mr. James R. R. Hamilton, M.R.C.V.S.

In reference to the passing of Mr. James Robert Roe Hamilton, which we regret to record above, Mr. J. Spreull, F.R.C.V.S., writes as follows from East London regarding his "late colleague and fellow student": "Mr. James Hamilton, who died here in East London on July 31st last, was a native of County, Roscommon, Ireland, and after studying at Trinity College emigrated to North Dakota where he tried ranching for six years but gave it up to enter the New Veterinary College, Edinburgh, from which he graduated on December 19th, 1894. He became a civil veterinary surgeon attached to the British Forces towards the end of the Boer War and thereafter transferred to the Veterinary Service of the O.F.S. The last nine years of his service under the Union Government were spent in Durban where he retired in 1924. He left a widow but no family.

Always genial and of a kindly disposition he was a great lover of animals."

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FOOT-AND-MOUTH DISEASE IN DORSET

The existence of foot-and-mouth disease was confirmed on Sunday last among cattle at West Morden, Dorset. The area subject to restrictions in the movement of animals lies principally in the county of Dorset, but small parts of the area are situated in the counties of Hampshire and Wiltshire.

ADDITIONAL PETROLEUM SUPPLIES FOR VETERINARY SURGEONS

List of Liaison Officers

In our last issue, we intimated that the President, N.V.M.A., had addressed a letter to the Mines Department and all Divisional Petroleum Officers, requesting that throughout the country there should be appointed Liaison Officers between veterinary surgeons and Divisional Petroleum Officers with a view to facilitating the provision of additional supplies of petrol for members of the veterinary profession. We are glad to be able to report considerable progress in this matter and the following is a list of the Divisions (intimating the areas covered and names and addresses of Divisional Petroleum Officers) in which appointments as Liaison Officers have been made to date, indicating the holders of these appointments, to whom application should be made with the particulars notified in our last issue.

Division	Liaison Officer
Northern Division.—Captain C. C. Webb, Dean Holme, Clayton Road, Jesmond, Newcastle-on-Tyne (Northumberland, Durham, and N. Riding of Yorkshire).	Mr. W. Lyle Stewart, M.R.C.V.S., Hon. Secretary, North of England Division, N.V.M.A., King's College, Newcastle-on-Tyne, 2.
North-Eastern Division.—Major G. T. Wright, Brunswick Sunday Schools, Wesley Street and Hartley Hill, Leeds (Yorkshire, less N. Riding).	Mr. A. J. Adams, B.Sc., M.R.C.V.S., Hon. Secretary, Yorkshire Division, N.V.M.A., "Lenaire," Rivock Avenue, Utley, Keighley, Yorks.
North Midland Division.—Lieut.-Colonel A. M. Cockshott, Mechanics Institute, North Church Street, Nottingham (Counties of Nottingham, Lincoln, Rutland, Northampton, Soke of Peterborough, Leicester, and Derby, less the areas of Borough of Glossop and New Mills and Whaley Bridge Urban District Councils, Borough of Buxton, and Chapel-en-le-Frith Rural District Council).	Mr. Lindsay Auchterlonie, M.R.C.V.S., Hon. Secretary, Derbyshire Division, N.V.M.A., 63, Ilkeston Road, Nottingham.
Eastern Division.—Mr. Grafton Pryor, Douglasbank, Lathom Road, Cambridge (Counties of Norfolk, Suffolk, Cambridge, Huntingdon, Isle of Ely, Bedford, Herts, and Essex, less that part of the Metropolitan Police Area lying within the two latter counties).	Mr. Harry P. Standley, Jun., M.R.C.V.S., Hon. Secretary, Eastern Counties Division, N.V.M.A., Orford Place, Norwich.
Herts and Essex Area.—Mr. J. Lindsay Allen, Congregational Sunday School, New London Road (corner of Friar Place), Chelmsford (Herts and Essex portion of the Eastern Division); and *London Division.*—Mr. F. E. M. Beatley, Broadway Congregational Hall, Brook Green Road, Hammersmith (London and Middlesex and those parts of Essex, Herts, Surrey, and Kent lying within the Metropolitan Area).	Mr. H. E. Bywater, M.R.C.V.S., Hon. Secretary, Central Division, N.V.M.A., 55, Cheyne Avenue, Snaresbrook, E. 18.
South-Western Division.—Mr. F. J. Salmon, Central Hall, Red Cross Street (off Old Market Street), Bristol, 8 (Counties of Gloucester, Wilts, Dorset—excluding the areas of Poole Borough, Wimborne Minster Urban District and Wimborne and Cranborne Rural District—Somerset, Devon, Cornwall, and Scilly Isles).	Mr. C. E. Perry, F.R.C.V.S., Hon. Secretary, Mid-West Division, N.V.M.A., "Woodlands," Staple Hill, Bristol.
Welsh Division.—Mr. W. Morgan, Dormie Café, Andrews Arcade, Queen Street, Cardiff (Counties of Cardigan, Radnor, Brecknock, Monmouth, Glamorgan, Carmarthen, and Pembroke).	Mr. T. H. Jones, M.R.C.V.S., Hon. Secretary, South Wales Division, N.V.M.A., Neuadd, Llandilo, Carmarthenshire.
North Wales Area.—Mr. B. A. Warner, Queen's Tower, Caernarvon Castle, Caernarvon (Counties of Anglesey, Caernarvon, Merioneth, Montgomery, Denbigh, and Flint).	Mr. H. V. Hughes, B.V.Sc., M.R.C.V.S., D.V.H., Hon. Secretary, North Wales Division, N.V.M.A., The University, Liverpool.
Midland Division.—Colonel W. E. H. Bradburn, St. Martin's Street, Five Ways, Edgbaston, Birmingham, 15 (Counties of Stafford, Warwick, Worcester, Hereford, and Salop).	Mr. H. W. Dawes, M.R.C.V.S., Hon. Secretary, Midland Counties Division, N.V.M.A., Camden House, High Street, West Bromwich.
North-Western Division.—Mr. R. H. Whitehorn, 76, Newton Street, Manchester, 1 (Counties of Cumberland, Westmorland, Lancaster, Chester, plus the area of the Borough of Glossop and New Mills and Whaley Bridge Urban District Councils, Borough of Buxton, and Chapel-en-le-Frith Rural District Council).	Mr. J. Holroyd, F.R.C.V.S., D.V.S.M. (Vict.), 1, Simmons Street, Blackburn.

DIVISION

South-East Scotland Division.—Mr. R. B. Crabb, 15, George Street, Edinburgh (Midlothian, East Lothian, West Lothian, Berwick, Roxburgh, Peebles, Selkirk, Dumfries, Fife, Kinross, Perth, and Clackmannan).

South-West Scotland Area.—Mr. W. Armour, 49, Queen's Street, Glasgow (Counties of Renfrew, Lanark, Argyll, Ayr, Bute, Dumbarton, Stirling, Kirkcudbright, and Wigtown).

LIAISON OFFICER

Mr. A. Gofton, F.R.C.V.S., Chief Veterinary Officer, Veterinary Department, Public Health Chambers, Johnston Terrace, Edinburgh, 1.

Mr. Alex. Thomson, M.R.C.V.S., Hon. Secretary, West of Scotland Division, N.V.M.A., 220, Albert Drive, Pollokshields, Glasgow, S.1.

COLONIAL VETERINARY SERVICE APPOINTMENTS

Announcement is made of the following first appointments in the Colonial Veterinary Service:—

BIGGAR, W. S., B.Sc., M.R.C.V.S., Veterinary Officer, Northern Rhodesia.

RANDALL, J. B., M.R.C.V.S., Veterinary Officer, Uganda.

TAYLOR, J. I., B.Sc., M.R.C.V.S., Veterinary Officer, Northern Rhodesia.

WHITE, D. G., B.Sc., M.R.C.V.S., Veterinary Officer, Tanganyika Territory.

PROMOTION

HIGGINS, Major R. H. C., M.B.E., M.R.C.V.S. (Veterinary Officer), Senior Veterinary Officer, Tanganyika Territory.

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AVIAN TUBERCULOSIS AND MEAT INSPECTION

The following quotation from "Avian Tuberculosis Infections" by Feldman (1938) is of interest for the opinion expressed on the attitude to be adopted towards meat inspection as applied to tuberculous poultry carcases. A recent paper by White and Ellis (*Vet. Rec.* 1939. 475) evoked some correspondence on this subject.

Pp. 444-5.

"The lack, at the present time, of efficient *post-mortem* inspection of all poultry intended for human consumption not infrequently results in carcases of tuberculous chickens and turkeys being received by the housewife who assumes that the birds she has purchased are healthy. Furthermore, viable and virulent tubercle bacilli may occasionally occur in the eggs from tuberculous hens.

"These facts are not sufficient, however, to warrant the assumption that the bacilli of avian tuberculosis should be considered a major hazard to human health. Rather, these organisms should be looked upon as possible sources of infection for human beings and this should engender a concept of food sanitation that would exclude, in so far as possible, articles of food containing or likely to contain virulent tubercle bacilli even though the bacilli are heterologous."

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LEGAL NOTES

Failure to Report Swine Fever.—At the West Ham Police Court on September 26th, Mrs. Brett, of Custom House, a smallholder, was fined £10 and £5 costs for failure to report suspected swine fever, for causing to be exposed on the highway pigs so affected and further with failing to make the required entries in the Movement of Animal (Records) Book. Mr. Hallett, her manager, was fined £5 for similar offences.

Mr. H. E. Bywater, M.R.C.V.S., prosecuting on behalf of the West Ham Corporation, said that Mrs. Brett was the owner and Mr. Hallett the manager of a business with a smallholding at Leyes Road, Custom House, West Ham. The business had been in existence for many years and the buying and selling of pigs was an essential feature of the business. On July 14th, 20 pigs were conveyed by a hired lorry from the piggeries at Leyes Road to Chelmsford Market where they were entered under a false name. On the same day other pigs were taken to the market in Mrs. Brett's own lorry and sold under her name. Eight of the 20 pigs were bought by Mrs. Cook, of Highwood, near Chelmsford, who noted that they appeared unwell in the market and, finding no improvement on getting them home, reported suspected swine fever to the police. They were subsequently examined by Mr. H. McShane, M.R.C.V.S., Chelmsford, who diagnosed swine fever and sent specimens to the Ministry of Agriculture Veterinary Laboratory where the diagnosis was confirmed. He was of the opinion that the pigs were so infected for at least a week before being exposed in the market. A deal of difficulty was experienced and delay was caused in tracing the ownership of these pigs and in consequence of the exposure of the pigs in the market further outbreaks of swine fever had resulted in various parts of Essex.

When the pigs were finally traced to Mrs. Brett's piggeries Mr. J. Mason, M.R.C.V.S., a veterinary inspector of the Ministry of Agriculture, visited the piggeries and although most of the pigs there appeared healthy, one isolated in a sty on its own, was obviously diseased and appeared to be suffering from chronic swine fever. During the course of this visit Mrs. Brett was requested to produce her Movement of Animals (Records) Book when it was noted that no entry had been made of the movement of the 20 pigs taken to Chelmsford Market on July 14th; neither was there any entry in respect of two pigs licensed on June 9th, to be moved from Chelmsford Market to Leyes Road. The entry in respect of the pigs moved on July 14th in Mrs. Brett's own lorry and entered under her own name in the market was in order.

The maximum penalty for failing to record the movement of the 20 pigs was £100, whils the penalty for the other offences was £50.

Mr. Malcolm Lynde, pleading guilty on the defendants' behalf, said Mrs. Brett had never

seen swine fever before although she had kept pigs for a number of years, and asked the magistrate to deal leniently with her owing to her financial position and the fact that she had relied on Hallett to look after the piggeries.

The magistrate, Mr. St. John Morrow, said it was a very serious case and it was a despicable thing to use a false name.

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BLOEMFONTEIN TURF CLUB: STEWARDS' RESIGNATION

The recent resignation of stewards of the Bloemfontein Turf Club—including that of the chairman, the vice-chairman and of the secretary, Lieut.-Colonel Wakefield Rainey, C.B.E., M.R.C.V.S.—was referred to at the annual general meeting of the Bloemfontein Turf Club.

In the course of the chairman's annual report it was stated that the essential reason for the resignations was a lack of confidence felt by those who resigned in the local executive of the Jockey Club in its new capacity as a virtual substitute for the executive stewards in Johannesburg in disciplinary matters.

"Those who have resigned believed that the maintenance of clean racing, which has been difficult enough in the past when all disciplinary cases were reviewed by the executive stewards of the Jockey Club, would be so difficult in future that they could not conscientiously retain their offices. The secretary resigned because it was action on his part which led to the testing of the local executive under the new organisation whereby the resignations have occurred. As he had been primarily responsible and because he agreed with the conclusions of the retiring stewards, he felt that he was in honour bound also to retire."

Going on to deal with the future outlook, the report stated:—

"Experience has now proved that with care and economy the Club should be able to pay its way so long as salaries do not have to be increased, and dilapidations on the racecourse do not become serious.

"In other respects, however, the future is uncertain because, without assured discipline, local racing must be increasing unattractive to the public who provide the money by means of which we race. And discipline can only be assured if the officials charged with the unpleasant but necessary duty of administering it are properly supported. Otherwise, it breaks down, and in the end, everything breaks down."

On the proposal of Mr. Dan Ingram, it was suggested to Colonel Rainey that he be asked to reconsider his resignation in view of his splendid services to the Club.

Colonel Rainey told the meeting that he would go into the matter of his resignation and see what steps he could honourably take to bring about Mr. Ingram's suggestion.

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By discouraging the production of the prime beef for which Scotland is justly famed throughout the world, the whole of our livestock industry—pedigree as well as commercial breeding—is endangered, and it will be no easy matter to recover lost ground. It is further endangered by the suspension of the Bull Licensing Act. A return to a policy which will encourage the breeding and feeding of prime-quality cattle must be made before it is too late. The Bull Licensing Act must be restarted.—*Scottish Farmer.*

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Members of the Chillingham Wild Cattle Association, which was formed to prevent the extinction of the famous wild white cattle on the Earl of Tankerville's Northumbrian estate, hope to continue to preserve the herd, but fear for the future if food should become scarce.

DISEASES OF ANIMALS ACTS, 1894 TO 1937, AND AGRICULTURE ACT OF 1937 (PART IV)

SUMMARY OF RETURNS

Period.	Anthrax.		Foot-and-Mouth Disease.		Parasitic§ Mange.		Sheep Scab.	Swine Fever.	
	Outbreaks confirmed.	Animals attacked.	Outbreaks confirmed.	Animals slaughtered as diseased or exposed to infection.	Outbreaks confirmed.	Animals attacked.	Outbreaks confirmed.	Outbreaks confirmed.	Swine slaughtered.
	No.	No.	No.	No.	No.	No.	No.	No.	No.
Period 1st to 15th Sept., 1939	16	32	4	267	1	1	1	153	113
Corresponding period in									
1938	19	22	2	169	—	—	4	52	39
1937	19	20	1	446	5	5	—	20	8
1936	17	18	1	69	5	5	4	40	37
Total 1st January to 15th Sept., 1939	563	632	67	7,360	32	72	167	1,734	1,210
Corresponding period in									
1938	599	959	162	20,633	42	72	120	495	381
1937	509	616	20	4,919	96	134	139	768	468
1936	329	389	5	448	91	233	167	1,396	995

NOTE.—The figures for the current year are approximate only.

§ Excluding outbreaks in Army Horses.